Office Action Summary	Application No.	Applicant(s)
	10/533,103	BOCHAROV ET AL.
	Examiner	Art Unit
	SATYANARAYANA GUDIBANDE	1654

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 December 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-26* is/are pending in the application.

4a) Of the above claim(s) *2,4 and 14-26* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 3 and 5-13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)	
1) ☐ Notice of References Cited (PTO-892)	4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)	5) ☐ Notice of Informal Patent Application
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.	6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election of group II invention (claim 3 along with linking claims 1 and 5-13) and election of SEQ ID NO: 10 as a species of the molecule and inflammation as the disease condition in the reply filed on 7/6/10 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Status of pending claims

Claims 1-26 are pending.

Claims 2 and 4 have been withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 7/6/10.

Claims 14-26 have been withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 7/6/10.

Claims 1, 3 and 5-13 are examined on the merit.

Any objections and/or rejections made in the office action mailed on 7/21/10 and not specifically discussed below in its original or modified form here are considered withdrawn.

Maintained Rejections

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claims 1, 3-8, 10, 11 and 13 remain rejected under 35 U.S.C. 102(e) as being anticipated by US 6,156,727 issued to Garber in light of Selzman, Ann Thorac Surg, 2001; 71:2066-2074. Response to applicant's arguments appears at the end of the reiterated rejection.

In the instant invention, applicants claim a method for treatment of inflammation comprising providing to a recipient a physiologically effective amount of a pharmaceutical composition of a molecule that targets SR-B1/CLA-1.

Applicants elect, Asp Trp Leu Lys Ala Phe Tyr Asp Lys Val Ala Glu Lys Leu Lys Glu Ala Phe Pro Asp Trp Leu Lys Ala Phe Tyr Asp Lys Val Ala Glu Lys Leu Lys Glu Ala Phe (SEQ ID NO: 10), a peptide as the molecule that is present in the pharmaceutical composition of the instant method.

The peptide SEQ ID NO: 10 of the instant application is disclosed by Garber and is known as 18A-Pro-18A, (SEQ ID NO: 1) wherein an amphipathic peptide 18A synthesized as a head-to-tail dimer with a proline incorporated (column 6, lines 38-40).

Garber discloses the peptide of instant invention as SEQ ID NO: 1 (column 6, column 17 and elsewhere in the document) and discloses that the pharmaceutical composition of the peptide (column 15, lines 1-3) and the composition is administered to fat sensitive mice that develops spontaneous atherosclerosis lesions (Example 11, column 13). Atherosclerosis lesion is caused by inflammation as illustrated by Selzman (Figure 3 and page 2072, column 2). This reads on the instant claims 1, 3, 5, 8 and 11. The amphipathic peptide 18A-Pro-18A competes with HDL for binding and HDL has been shown to deliver cholesterol to the cells through class B scavenger receptor SRB1. This reads on the instant claims 7 and 10. Garber also discloses that a dosage of peptide to be injected was selected based on the in vivo studies conducted using 18A peptide to inhibit the LPS-induced toxicity in mice (Example 3, lines 27-30). This reads on the instant claim 6. Garber discloses the administration of SEQ ID NO: 10 of the instant invention to fat sensitive mice and hence it inherently exhibits the Kd lower than 10^{-7} to SR-B1 receptor. Hence, Garber anticipates the instant invention.

Response to Arguments

1. Applicants argue that office has drawn incorrect conclusion from Selzman that atherosclerosis being caused by inflammation. Applicants argue that Selzman does not teach all phases of atherosclerosis and the formation of atherosclerotic plaques caused by inflammation. Applicants further states that Selzman teaches atherosclerosis is a disease of many phases

including non-inflammatory phase, and can be initiated in childhood. Applicants acknowledges that the initial lipid accumulation phase which eventually leads to injury of endothelium leading to an inflammatory response. However, applicants submit that atherosclerosis does not involve inflammation of at all stages, and early are characterized by lipid deposition that eventually leads to inflammatory response (page 7-8 of response filed 12/21/10).

Applicant's arguments filed 12/21/10 have been fully considered but they are not persuasive. It should be noted that Selzman has been used in the rejection as an evidentiary reference that teaches that atherosclerosis lesion is caused by inflammation. The primary reference of Garber clearly illustrates that the peptide is administered in a pharmaceutical composition to treat atherosclerosis in an animal (claim 3 of Garber). Hence treatment of atherosclerosis as illustrated by Garber would treat the underlying condition of inflammation when administered to patients.

2. Applicants argue that Garber teaches the use of SEQ ID NO: 1 for the purpose of preventing lipid buildup. Applicants state that Garber teaches that cholesterol-binding protein ApoA-I can protect against formation of lipid deposits in mice susceptible to diet-induced atherosclerosis. Applicants further argue that an extensive review of the teachings of Garber and Selzman show that atherosclerosis is a complex disease which occurs in phases and **several of which do not comprise an inflammatory response**. Applicants further states that the applied citations do not teach 18A-Pro-18A (SEQ ID NO: 1) of Garber as an anti-inflammatory agent but merely as an atherosclerotic protective one. Applicants further add that the Garber and Selzman citations do not teach an anti-inflammatory properties of 18A-Pro-18A by inherency.

Applicant's arguments filed 12/21/10 have been fully considered but they are not persuasive. Applicants characterization that atherosclerosis is a complex disease which occurs in phases and **several of which do not comprise an inflammatory response** is not persuasive because applicants seems to be arguing facts that are not present in the instant claims. Moreover, the instant specification on page 5, line 23-25 discloses that "[B]oth clinical and experimental data support considering atherosclerosis as a chronic inflammatory disorder associated with endothelial and cholesterol balance dysfunction". This is clearly contradictory to the applicant's afore-quoted argument. Also as mentioned earlier Garber clearly illustrates that the peptide is administered in a pharmaceutical composition to treat atherosclerosis in an animal (claim 3 of Garber). Hence treatment of atherosclerosis as illustrated by Garber would treat the underlying condition of inflammation when administered to patients.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later

invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 3 and 5-13 remain rejected under 35 U.S.C. 103(a) as being unpatentable over US 6,156,727 issued to Garber in view of US 6,664,230 issued to Fogelman in light of Selzman, Ann Thorac Surg, 2001;71:2066-2074. Response to applicant's arguments appears at the end of reiterated rejection.

In the instant invention, applicants claim a method for treatment of inflammation comprising providing to a recipient a physiologically effective amount of a pharmaceutical composition of a molecule that targets SR-B1/CLA-1.

Applicants elect, Asp Trp Leu Lys Ala Phe Tyr Asp Lys Val Ala Glu Lys Leu Lys Glu Ala Phe Pro Asp Trp Leu Lys Ala Phe Tyr Asp Lys Val Ala Glu Lys Leu Lys Glu Ala Phe (SEQ ID NO: 10), a peptide as the molecule that is present in the pharmaceutical composition of the instant method. The peptide SEQ ID NO: 10 disclosed by Garber is also known as 18A-Pro-18A, wherein an amphipathic peptide 18A synthesized as a head-to-tail dimer with a proline incorporated (column 6, lines 38-40).

Garber discloses the peptide of the instant invention SEQ ID NO: 1 (column 6, column 17 and elsewhere in the document) and discloses that the pharmaceutical composition of the peptide (column 15, lines 1-3) and the composition is administered to fat sensitive mice the atherosclerosis lesions (Example 11, column 13). Atherosclerosis lesion is caused by inflammation as illustrated by Selzman (Figure 3 and page 2072, column 2). This reads on the instant claims 1, 3, 5, 8 and 11. The amphipathic peptide 18A-Pro-18A competes with HDL for binding and HDL has been shown to deliver cholesterol to the cells through class B scavenger

receptor SRB1. This reads on the instant claims 7 and 10. Garber also discloses that a dosage of peptide to be injected was selected based on the in vivo studies conducted using 18A peptide to inhibit the LPS-induced toxicity in mice (Example 3, lines 27-30). This reads on the instant claim 6. Garber discloses the administration of SEQ ID NO: 10 of the instant invention to fat sensitive mice and hence it inherently exhibits the Kd lower than 10^{-7} to SR-B1 receptor.

Garber does not disclose peptides composed of D-amino acid residues.

Fogelman discloses peptide that comprises of essentially every enantiomeric amino acid is a D-amino acid (column 17, line 55 to column 18, line 8). This reads on the instant claims 9 and 12. The peptide SEQ ID NO: 1, disclosed by Fogelman is 18A peptide of Garber. Fogelman also discloses that peptides synthesized with D-amino acid residues are more resistant to digestion in stomach (in vivo studies) and hence was able to perform better than the peptides synthesized with L-amino acids. However, the performance of both L- and D-peptides were comparable in in vitro studies. This is indicative of the fact that peptides comprising of D-amino acids were resistant to degradation in stomach.

It would have been obvious to one of ordinary skill in the art to combine the teachings of Garber and Fogelman to arrive at the instant invention as Garber discloses the method of treating inflammation with the elected peptide of the instant peptide and Fogelman teaches the peptides wherein L- isomers were replaced with D-isomers of amino acids residues. One would have been motivated to combine the teachings of Garber and Fogelman in light of information available form Selzman given the fact that peptides synthesized with D-amino acids are resistant to degradation in stomach and are as effective as peptides made of L-amino acids. A reference is good not only for what it teaches by direct anticipation but also for what one of ordinary skill in

the art might reasonably infer from the teachings. (In re Opprecht 12 USPQ 2d 1235, 1236 (Fed Cir. 1989); In re Bode 193 USPQ 12 (CCPA) 1976). In light of the forgoing discussion, the Examiner concludes that the subject matter defined by the instant claims would have been obvious within the meaning of 35 USC 103(a). From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Response to Arguments

Applicants argue that "As discussed in the anticipation rejection and incorporated herein, it is submitted in fact Garber in light of Selzman does not teach the instant pepide for the treatment of inflammation". Applicants further add that no anti-inflammatory roles for these peptides were demonstrated. With regards to Fogelman citation applicants' states that Fogelman does not teach the missing element, i.e., 18A-Pro-18A is useful for treating inflammation.

Applicant's arguments filed 12/21/10 have been fully considered but they are not persuasive. As mentioned earlier, Garber clearly illustrates that the peptide SEQ ID NO: 1 (18A-Pro-18A) is administered in a pharmaceutical composition to treat atherosclerosis in an animal (claim 3 of Garber) and the instant specification recognizes that atherosclerosis is an inflammatory disease condition. Hence treatment of atherosclerosis as illustrated by Garber would treat the underlying condition of inflammation when administered to patients. With respect to Fogelman it should be noted that the citation discloses the D-isomer of peptide SEQ

ID NO: 1 of Garber and the peptide synthesized with D-amino acid residues are more resistant to digestion in the stomach and are able perform better compared to peptides synthesized using L-amino acids. Fogelman citation was used to reject instant claims 9 and 12 that are drawn to peptides of instant invention composed of solely D-amino acids.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a). Applicant's arguments as presented on reply filed on 12/21/10 did not overcome the rejection on record.

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Satyanarayana R. Gudibande whose telephone number is 571-272-8146. The examiner can normally be reached on M-F 8-4.30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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